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### REMARKS

Claims 1-10 and 12-43 are pending in the present application. Claims 1, 9, 10, 13 and 18 have been amended. Support for the amendments is found throughout the specification. No new matter has been added by virtue of these amendments and their entry is respectfully requested. Claims 14-17 have been cancelled. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

#### *Claim Rejections Under 35 U.S.C. § 112.*

Claims 1, 9-10 and 12-18 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification is not enabling for analyzing the brain tissue sample for overexpression of any "VEGF-D marker" wherein the VEGF-D marker is any VEGF-D protein, any native VEGF-D protein, any proteolytic cleavage product of any VEGF-D precursor protein and consists of any VEGF-D homology domain, any probe which comprises any antibody, any polyclonal antibody, any monoclonal antibody, any anti-VEGF-D homology domain antibody as set forth in claims 1, 9-10, and 12-18. Applicants respectfully traverse.

However, in order to compact prosecution and expedite allowance, Applicants have amended the claims as per the Examiner's recommendation. These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 1, 9-10, and 12-18 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

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reasonable convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse. The Examiner asserts that the specification does not reasonably describe any and all probe, and any and all antibody that binds to any VEGF-D, any native VEGF-D protein, any proteolytic product of any VEGF-D precursor protein which consists of any VEGF-D homology domain for the claimed method of detecting any and all cancer in any brain tissue.

Although Applicants disagree, applicants have amended the claims as per the Examiner's recommendation. These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 1, 9-10 and 12 are rejected under 35 U.S.C. § 112, second paragraph as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

Applicants have amended the claims to include the step "contacting the tissue sample with a labeled antibody that binds specifically to human VEGF-D." (See, page 36 of the instant specification as cited by the Examiner). These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter. These amendments are deemed to overcome the Examiner's rejections.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

*Claim Rejections Under 35 U.S.C. § 103.*

Claims 1, 9-11 and 13-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,235,713 B1 (filed Aug 1997; PTO 892) in view of U.S. Patent No.

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5,874,290 (Feb 1999; PTO 892) and Hamel et al (*Acta Neurochirurgica* 142:113-138, 2000; PTO 892).

Applicants respectfully disagree and traverse the rejection.

As the Examiner states, the references do not teach a method of detecting cancer in a brain tissue sample. The '713 patent does not teach or suggest that VEGF-D is detected in brain tissue samples. Hamel *et al* do not teach or disclose the detection of VEGF-D in glioblastomas detected in brain tissue samples. Considering that different VEGFs have different chromosomal localizations, one of ordinary skill in the art would not expect that just because one type of VEGF is found in cancer, the detection of another factor is expected or obvious. It would not be obvious to one of skill in the art that VEGF-D is detectable in human brain tissue samples. The '290 patent does not teach or disclose that VEGF-D is over-expressed in tumors. VEGF was detected in some brain tumors but the '290 patent does not teach or disclose detection and over-expression of VEGF-D as a diagnostic marker of brain tumors isolated from human brain tissue samples. As stated in previous responses, the '290 patent utilized established cell lines for detection of the D2-2 gene. (See, for example, column 43, lines 49-62). Applicants submit that fetal brain tissue is not a tumor as suggested by the Examiner and consequently cannot be used as a tool to diagnose brain tumors.

However, in order to expedite prosecution, Applicants have amended the claims to recite "brain tissue sample", "native VEGF-D" and "full-length native VEGF-D." These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter. These amendments are deemed to overcome the Examiner's rejections.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 10, 12 and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of U.S. Patent No.

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5,874,290 (of record, Feb 1999; PTO 892) as applied to claims 1, 9 and 13-17 and further in view of Stacker et al (of record, J. Biol. Chem. 274(45):32127-32136; Nov 1999; PTO 1449) and Achen et al (of record, Eur. J. Biochem. 267:2505-2515, May 2000; PTO 1449).

Applicants respectfully traverse.

As the Examiner has stated, that the instant invention differs in that the method for detecting cancer in a brain tissue sample wherein the VEGF-D protein is a native VEGF-D protein. Claim 18 differs in that the method for detecting cancer in a brain tissue sample, wherein the monoclonal antibody is an anti-VEGF-D homology domain antibody.

Arguments regarding the combined teachings of '713 and '290 and Hamel have been discussed *supra*, and for the sake of brevity will not be repeated here. Neither Stacker et al, nor Achen et al, standing alone or in combination teach the detection of a native protein VEGF-D homology domain in brain cancer. None of the references teach the detection of VEGF-D in the brain nor, was the form of VEGF-D in the brain known prior to applicants invention.

However, in order to expedite prosecution, Applicants have mended the claims. These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter. These amendments are deemed to overcome the Examiner's rejections.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the rejection.

### CONCLUSION

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1, 9, 10 and 12-18 define patentable subject matter and is in condition for allowance. Accordingly, Applicant respectfully requests allowance of these claims.

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Applicants have made every effort to present claims which distinguish over the cited art, and it is believed that all claims are now in condition for allowance. However, Applicants request that the Examiner call the undersigned (direct line 561-671-3666) if anything further is required by the Examiner prior to issuance of a Notice of Allowance for all claims.

This response is being filed within the shortened statutory period and as such, Applicants believe no extensions of time or fees are due with the submission of this paper. Although, Applicants believe that no petition of time or fees are due, please consider this submission as a petition for retroactive extension of time. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for a one month retroactive extension of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing, or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMANTENTERFITT

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